2,5-Cyclohexedienones. 4. Reactions of 4-Bromo-2, 4, 6-tri-tert-butyl-2, 5-cyclohexadien-1-one with Glycols

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2,5-Cyclohexedienones. 4. Reactions of 4-Bromo-2,4,6-tri-tert-butyl-2,5-cyclohexadien-1-one with Glycols

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Reactions of 4-bromo-2, 4, 6-tri-t-butyl-2, 5-cyclohexadien-1-one (**1**) with ethylene glycol (**2a**), and di-(**2b**) and triethylene glycol (**2c**) were carried out under various conditions. Pyridine can act as a good catalyst for the preparation of the corresponding dienoxy alcohols (**3a-c**). However, ω, ω'-bis (4-oxo-2, 5-cyclohexadien-1-yl) ethers (**4a-c**) were obtained in considerable yields only when α-picoline was used as a catalyst.

In a series of papers, we have shown, as illustrated in Scheme 1 below, a new and convenient method for the selective preparation of o- and p-substituted phenols by utilizing a reaction of 4-bromo-2, 4, 6-tri-tert-butyl-2, 5-cyclohexadien-1-one (**1**)[1], which can be easily prepared by a bromination of 2, 4, 6-tri-t-butylphenol (**5**), with nucleophilic reagents such as sodium phenolate[2], amines[3], alcohols[4], and pyridines[5].

In this paper is reported the reaction of **1** with ethlene glycol (**2a**) and di-(**2b**)-and triethylene glycol (**2c**). The results are summarized in Scheme 2 and the **Table 1.**

When dienone (**1**) was heated in a large excess amount of glycol (**2**) under a stream of nitrogen with stirring at 110°C (bath temperature) in the presence of pyridine (in the molar ratio of 2 : 1 to **1**), the corresponding dienoxy alcohol (**3**) was obtained in ca. 70% yield. It was also found that ω,ω'-bis (4-oxo-2, 5-cyclohexadien-1-yl) ethers **4a** and **4b** were obtained in poor yields as minor products in the cases of **2a** and **2b**, respectively, but not from **2e**, even though these reactions were carried out in a large excesses of glycols[6]. Furthermore, an interesting phenomenon was observed when the reactions were carried out without stirring, namely, the yields of **4a** and **4b** increased from 0.4% to 19% and from 0.1% to 6%, respectively. In the case of **2c**, however, there was identified scarcely any corresponding compound **4**, even without stirring. It is not yet completely clear why such different results are obtained, but we might say that the difference may be due to the solubility of **1** in glycols used, since **1** is only slightly soluble in **2a**, somewhat soluble in **2b**, but easily soluble in **2c** under the reaction conditions.

The structures of the products **3a-3c**, **4a** and **4b** are fully supported by their elemental analysis, ^{1}H-nmr, ir- and mass spectra.

It has already been reported[4] that the reaction of **1**, **2a** and pyridine in molar ratio 1 : 1-2 : 2, where the possibility for the formation of **4a** seemed to be preferred judged by the molar ratio, afforded the unexpected product, 1-(3, 5-di-t-butyl-2-hydroxyphenyl)pyridinium bromide (**8**) in yield of 43% together with **5**, 2, 6-di-tert-butylbenzoquinone

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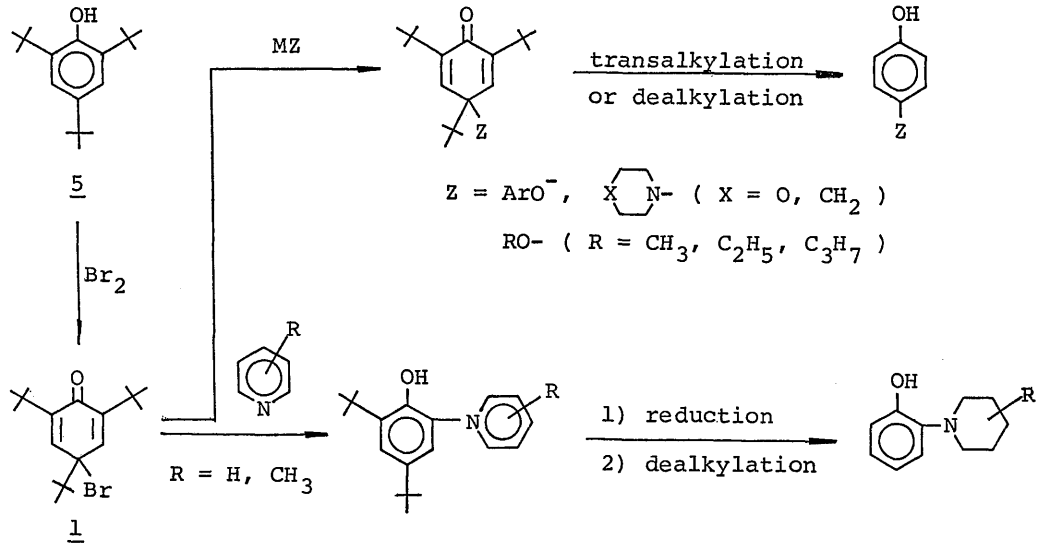
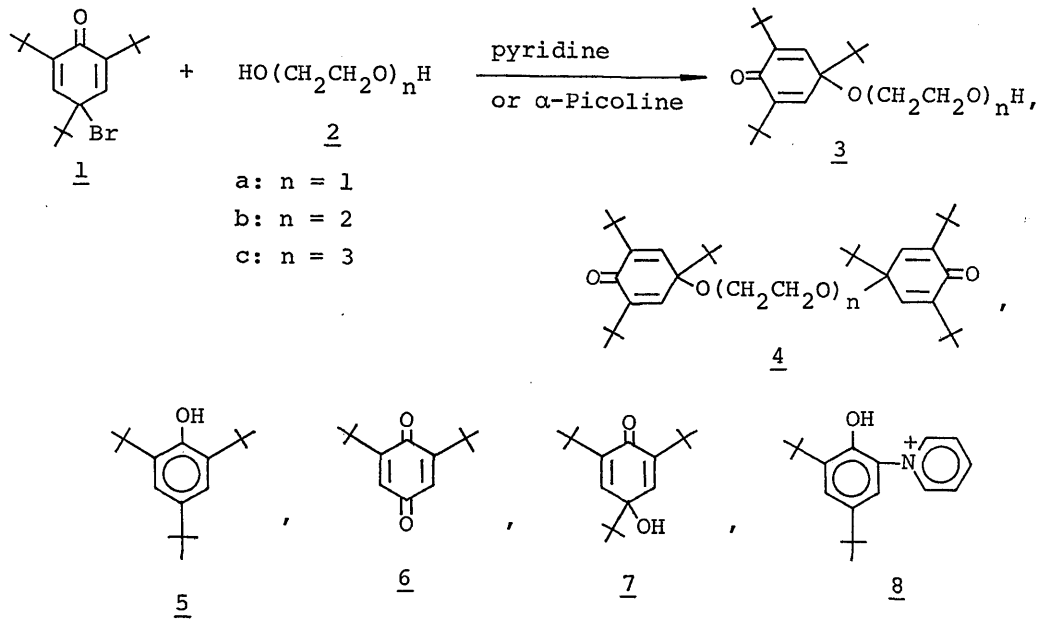


Scheme 1



Scheme 2

(**6**) and 2, 4, 6-tri-t-butyl-4-hydroxy-2, 5-cyclohexadien-1-one (**7**) as minor products, but not **4a**. It was now, however, found that in this reaction when α-picoline was used instead of pyridine, the expected product **4a** could be obtained in yield of 38% besides **3a**, **5**, **6** and **7** in 38, 0.1, 2 and 2% yields, respectively. And it was observed in the case of **2b** that on the formation of **4b**, the yield increased from 6% to 10% (see run 5 and 6). Furthermore, it was observed

Table 1. Reaction of 4-Bromo-2, 4, 6-tri-t-butyl-2, 5-cyclohexadien-1-one (**1**) with Glycols in the Presence of Pyridine[a].

Run	2	Products (Yield, %)[b]
1	a	**3a**(70), **4a**(0.4), **5**(0.1)
2[c]	a	**3a**(50), **4a**(19), **5**(4)
3[d]	a	**3a**(34), **4a**(38), **5**(0.1), **6**(2), **7**(2)
4	b	**3b**(68), **4b**(0.1), **5**(7)
5[c]	b	**3b**(64), **4b**(6), **5**(7)
6[d]	b	**3b**(44), **4b**(10), **5**(19), **6**(0.9), **7**(13)
7	c	**3c**(73), **5**(4)
8[c]	c	**3c**(72), **5**(5)
9[d]	c	**3c**(51), **4c**(7), **5**(20), **6**(1.4), **7**(5.4)
10[e]	a	**3a**(23), **5**(17), **6**(0.9), **7**(5), **8**(45)

a) All reactions were carried out in the conditions where a mixture of **1** (6.8 g, 20 mmoles), glycol (**2**) (50 ml) and pyridine (3.4 ml, 40 mmoles) were heated in an oil bath at ca. 110°C for 6hr under nitrogen atmosphere with stirring magnetically, unless otherwise indicated.
b) The yields, based on **1**, isolated were shown.
c) Without stirring.
d) α-Picoline instead of pyridine was used in this case, the molar of **1**, **2** and α-picoline =1 : 2 : 2.
e) From M. Tashiro and G. Fukata, Heterocycles, **12**, 1551 (1979).

in the case of **2c** that **4c**, which had not been formed under any other conditions where pyridine was used, could be obtained in yield of 7 % besides the other products. Such interesting difference between pyridin and α-picoline on the formation of **4** might reflect steric factors around the nitrogen atoms on their rings.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were mersered on a Nippon Bunko IR-A spectrophotometer as KBr pellets or as liquid films on NaCl pellets. ^{1}H-NMR spectra were determined at 60 MHz on a Hitachi R-20 spectrometer with TMS as an internal reference. Mass spectra were recorded on a Hitachi R-4 mass spectrometer at 70 eV using a direct inlet system.

General Procedure for the reaction of 1 with Glycol.-A (Run 1, 2, 4, 5, 7 and 8): A mixture of **1** (6.8 g, 20 mmoles), glycol (**2**) (50 ml) and pyridine (3.4 ml, 40 mmoles) were heated in an oil bath at ca. 110°C for 6hr under nitrogen atmosphere with stirring (or without stirring). After the reaction mixture was cooled down to room temperature, it was extracted with benzene (3×100 ml). The benzene layer was washed with water and after dried it with sodium sulfate, it was evaporated in vacuo to leave a residue. The residue was washed with cold methanol to give compound **4** as crystals. The residue, which was leaved by evaporation of the methanol, was subject to column chromatography on silica-gel (Wako gel C-300) using at first hexane (A) and then benzene (B) and finally ethyl acetate (C) as eluents. Compounds **5** and **6** were obtained from fraction A, **7** and **4** were isolated from fraction B and all of **3** was eluted from fraction C.

B (Run 3, 6 and 9): A mixture of **1** (3.4 g, 10 mmole), glycol (**2**) (20 mmole) and α-picoline (1.86 g, 20 mmole) was treated and worked up as described above.

Physical and spectral data of the pro-

ducts are as the following. The yields of the products are shown in **Table.**

2-(1, 3, 5-tri-t-Butyl-4-oxo-2, 5-cyclohexadien-1-oxy) ethanol (3a): viscous colorless oil, IR (NaCl): 3450, 1665, 1645, 1635 (sh) cm^{-1}. ^1H-NMR ($CDCl_3$): δ 0.95 (s, 9H), 1.26 (s, 18H), 2.0 (b, 1H; disappeared with D_2O), 3.35, 3.70 (each t, 2H, J= 6 Hz), 6.55 (s, 2H). Mass spectrum m/e: 322 (M^+).

Anal. Calcd for $C_{20}H_{34}O_2 \cdot 1/3\,H_2O$: C, 73.13; H, 10.64.

Found: C, 73.27; H, 10.48.

3-Oxa-5-(1, 3, 5-tri-t-butyl-4-oxo-2, 5-cyclohexadien-1-oxy) pentanol (3b): viscous colorless oil, IR (NaCl): 3450, 1665, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$): δ 0.95 (s, 9H), 1.25 (s, 18H), 2.16 (b, 1H; disappeared with D_2O), 3.36–3.76 (m, 8H), 6.56 (s, 2H). Mass spectrum m/e: 366 (M^+). Anal. Calcd for $C_{22}H_{38}O_4 \cdot 1/3\,H_2O$: C, 70.93; H, 10.46.

Found: C, 71.02; H, 10.30.

3, 6-Dioxa-8-(1, 3, 5-tri-t-butyl-4-oxo-2, 5-cyclohexadien-1-oxy) octanol (3c): viscous colorless oil, IR (NaCl): 3450, 1665, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$): δ 0.93 (s, 9H), 1.22 (s, 18H), 2.50 (b, 1H; disappered with D_2O), 3.30–3.80 (m, 12H), 6.56 (s, 2H). Mass spectrum m/e: 410 (M^+). Anal. Cacd for $C_{24}H_{42}O_5 \cdot 1/3\,H_2O$: C, 69.19; H, 10.32.

Found: C, 69.39; H, 10.10.

1, 2-Bis (1, 3, 5-tri-t-butyl-4-oxo-2, 5-cyclohexadien-1-oxy) ethylene (4a): mp 168.5–170 °C, colroless prisms (MeOH). IR (KBr): 1665, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$): δ 0.95 (s, 18H), 1.24 (s, 36H), 3.32 (s, 4H), 6.50 (s, 4H). Mass spectrum m/e: 582 (M^+).

Anal. Calcd for $C_{38}H_{62}O_4$: C, 78.30; H, 10.72.

Found: C, 78.16; H, 10.80.

1, 5-Bis (1, 3, 5-tri-t-buty-4-oxo-2, 5-cyclohexadien-1-oxy)-3-oxa-pentane (4b): mp 84.5–85.0°C, colorless plates (MeOH-H_2O). IR (KBr): 1665, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$): δ 0.96 (s, 18H), 1.26 (s, 36H), 3.43, 3.67 (each m, 4H), 6.62 (s, 4H). Mass spectrum m/e: 626 (M^+). Anal. Calcd for $C_{40}H_{66}O_5$: C, 76.63; H, 10.61.

Found: C, 76.54; H, 10.64.

1, 8-Bis (1, 3, 5-tri-t-butyl-4-oxo-2, 6-cyclohexadien-1-oxy)-3, 6-dioxaoctane (4c): mp 77–78°C, colorless prisms (MeOH-H_2O). IR (KBr): 1665, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$): δ 0.92 (s, 18H), 1.22 (s, 36H), 3.38, 3.60 (each t, 4H, J=5 Hz), 3.66 (s, 4H), 6.52 (s, 4H). Mass spectrum m/e: 670 (M^+).

Anal. Calcd for $C_{42}H_{70}O_6$: C, 75.18; H, 10.52.

Found: C, 75.27; H, 10.64.

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6) When equimolecular amount of ethylene glycol to one mole of **1** was used in the presence of pyridine, the unidentified compound was obtained but not **4a**.